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EXAMINER	
NEGIN, RUSSELL SCOTT	
ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 08/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/620,765	CASTLE ET AL.	
	Examiner	Art Unit	
	Russell S. Negin	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-56* is/are pending in the application.

4a) Of the above claim(s) *11-45 and 56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,46-53 and 55* is/are rejected.

7)☒ Claim(s) *54* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/13/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I (claims 1-10 and 46-55) in the reply filed on 30 May 2006 is acknowledged. The traversal is on the ground(s) that the classifications for Groups I and III are identical. In addition, the applicants argue that the method of Group III is dependent on the method of Group I. This is not found persuasive because identical classifications do not necessarily signify non-divergent subject matter. In this case, the extra feature of data normalization makes Group III distinct from Group I.

The requirement is still deemed proper and is therefore made FINAL.

Applicant's election with traverse of at least 10 cell or tissue types and at least 10 genes in the reply filed on 30 May 2006 is acknowledged. The traversal is on the ground(s) that the species are not independent or distinct. This is found to be persuasive, and the species are rejoined.

The requirement is still deemed proper and is therefore made FINAL.

Claims 11-45 and 56 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Group, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 30 May 2006.

Specification

It is noted that this application appears to claim subject matter disclosed in prior Application No. 60/396,145, filed 17 July 2002. A reference to the prior application must be inserted as the ***first sentence(s) of the specification*** of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e), 120, 121, or 365(c). See 37 CFR 1.78(a). For benefit claims under 35 U.S.C. 120, 121, or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of all nonprovisional applications. If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference to the prior application must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be

accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Paragraphs [0017], [0022], and [0026] contain embedded hyperlinks.

Claim Objections

Claim 54 is objected to under 37 CFR 1.75(c) as being in improper form because a dependent claim cannot be dependent on itself. Accordingly, the claim 54 will not be further treated on the merits.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4-10, 46, and 49-53 are rejected under 35 U.S.C. 103(a) as being anticipated by Roman et al. [Toxicology and Applied Pharmacology, volume 150, pages

228-239, 1998] in view of Wohlgemuth et al [US PGPUB 2004/0009479 A1, Application 10/131,827].

Claims 1, 4-8, 10, 46, and 49-53 state:

1. A method of identifying at least one gene that is consistently expressed across different cell or tissue types in an organism, comprising: (a) preparing gene expression profiles for different cell or tissue types from the organism; (b) calculating the percent variability of expression using a one-factor or two-factor ANOVA analysis for at least one gene in each of the profiles across the different cell or tissue types; and (c) selecting any gene whose percent variability of expression indicates that the gene is consistently expressed across the different cell or tissue types.

4. A method of claim 1, wherein the different cell or tissue types comprise greater than about 10 different cell or tissue types.

5. A method of claim 1, wherein the different cell or tissue types comprise greater than about 25 different cell or tissue types.

6. A method of claim 1, wherein the different cell or tissue types comprise greater than about 50 different cell or tissue types.

7. A method of claim 4, wherein the cell or tissue types comprise normal and diseased cell or tissue types.

8. A method of claim 1, wherein the organism is a mammal.

9. A method of claim 8, wherein the mammal is a rat.

10. A method of claim 1, wherein the expression profiles are generated by querying a gene expression database for the expression level of at least one gene in different cell or tissue types from the organism or from a cell line.

46. A method of identifying at least one gene that is consistently expressed across different cell or tissue types in an organism or cell line, comprising: (a) querying a gene expression database for the expression level of at least one gene in different cell or tissue types from the organism or cell lines; (b) calculating the percent variability of expression using a one-factor or two-factor ANOVA analysis for said at least one gene across the different cell or tissue types or cell lines; and (c) identifying at least one gene whose percent variability of expression indicates that the gene is consistently expressed across the different cell or tissue types or cell lines.

49. A method of claim 46, wherein the different cell or tissue types comprise greater than about 10 different cell or tissue types.

50. A method of claim 46, wherein the different cell or tissue types comprise greater than about 25 different cell or tissue types.

51. A method of claim 46, wherein the different cell or tissue types comprise greater than about 50 different cell or tissue types.

52. A method of claim 46, wherein the cell or tissue types comprise normal and diseased cell or tissue types.

53. A method of claim 46, wherein the organism is a mammal.

The article of Roman et al, is entitled, "Responsiveness of the Adult Male reproductive tract to 2,3,7,8-Tetrachlorodibenzo-p-dioxin exposure." Figure 1 on page 230 illustrates the organs being sampled for genetic expression analysis. In Figure 2, Roman et al illustrates consistent expression across several organs of the 105 kDa band of rat AhR in Figure 2A and the 86 kDa band of rat ARNT in Figure 2B. The gene expression profiles are prepared by Western blot analysis, and the particular bands are selected because they correspond to genes that are consistently expressed across various organs.

However, Roman et al does not teach the statistical analysis claimed in the instant set of claims.

The application of Wohlgemuth, entitled, "Methods and compositions for diagnosing or monitoring autoimmune and chronic inflammatory diseases," states in the abstract, "Methods of diagnosing or monitoring an autoimmune or chronic inflammatory disease, particularly SLE in a patient by detecting the expression level of one or more genes or surrogates derived therefrom in the patient are described...."

Paragraph [0007] of Wohlgemuth et al continues:

> In order to meet these needs, the present invention identifies genes and gene sets that have clinical utility as diagnostic tools for the management of transplant recipients, lupus patients and patients with a variety of chronic inflammatory and autoimmune diseases. The present invention is thus directed to a method of diagnosing or monitoring chronic autoimmune or inflammatory disease in a patient. The method of the invention involves detecting in a patient expression of one or more genes such as those genes depicted in Table 8 and Table 10A and surrogates derived therefrom. Exemplary surrogates are provided in Table 10C. The present invention is further directed to a method of diagnosing or monitoring an autoimmune or chronic inflammatory disease in a patient by detecting the expression level of one or more genes or surrogates derived therefrom in said patient to diagnose or monitor the autoimmune or chronic inflammatory disease in the patient wherein said genes include a nucleotide sequence selected from SEQ ID NO: 41; SEQ ID NO:328; SEQ ID NO:668; SEQ ID NO:855; SEQ ID NO:981; SEQ ID NO:1001; SEQ ID NO:1003; SEQ ID NO:1025; SEQ ID NO:1035; SEQ ID NO:1227; SEQ ID NO:1341; SEQ ID NO:1390; SEQ ID NO:1436; SEQ ID NO:1535; SEQ ID NO:1750; SEQ ID NO:2102; SEQ ID NO:2331; SEQ ID NO:2386; SEQ ID NO:2412; SEQ ID NO:2560; SEQ ID NO:2648; SEQ ID NO:2895, SEQ ID NO:3249; SEQ ID NO:3305; SEQ ID NO:3541;SEQ ID NO:3692; SEQ ID NO:3701; SEQ ID NO:3741; SEQ ID NO:3825; SEQ ID NO:3827; SEQ ID NO:3832; SEQ ID NO:4149; SEQ ID NO:4400; SEQ ID NO:4601; SEQ ID NO:4604; SEQ ID NO:4631; SEQ ID NO:4637; SEQ ID NO:5067; SEQ ID NO:5074; SEQ ID NO:5468; SEQ ID NO:5531; SEQ ID NO:5607; SEQ ID NO:6382; SEQ ID NO:6956; SEQ ID NO:7238; SEQ ID NO:7330; SEQ ID NO:7641; SEQ ID NO:8015 and SEQ ID NO:8095.

Tables 10A and 10C together illustrate many different biomolecules. The objective of Wohlgemuth et al is to diagnose a disease by consistently by examining a plurality of genes in a plurality of tissue types. As stated in the last sentence of the abstract of Wohlgemuth et al, "Diagnostic oligonucleotides for diagnosing or monitoring chronic inflammatory disease, particularly SLE infection and kits and systems containing the same are also described."

Wohlgemuth et al explains how ANOVA is used to analyze differences in gene expression. As stated in paragraph [0217], "Differences in gene expression across multiple related groups may be assessed using an Analysis of Variance (ANOVA), a method well known in the art."

Additionally, Figure 5B illustrates an application of statistical analyses to healthy and lupus patients.

Paragraph [0135] of Wohlgemuth et al explains that mice are a type of animal on which the genetic analysis can be performed (along with other types of mammals including humans).

Tables 10A and 10C are interpreted as databases of genes from which to observe expression levels in the different types of cells.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify Roman et al. in view of Wohlgemuth et al because while both use genetic expression analysis to examine consistency across a range of samples, in Roman et al. these samples are in the same organism, whereas in Wohlgemuth et al the samples are different organisms but with the advantage of complex statistical analysis utilized to determine the extent of consistency (and as a result, the diagnosis of lupus).

Claims 1-3 and 46-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roman et al in view of Wohlgemuth et al. as applied to claims 1, 4-10, 46, and 49-53 above in further view of Michelson et al [The Biostatistics Cookbook, Kluwer Academic Publishers, Boston, 1996, pages 77-89].

1. A method of identifying at least one gene that is consistently expressed across different cell or tissue types in an organism, comprising: (a) preparing gene expression profiles for different cell or tissue types from the organism; (b) calculating the percent variability of expression using a one-factor or two-factor ANOVA analysis for at least one gene in each of the profiles across the different cell or tissue types; and (c) selecting any gene whose percent variability of expression indicates that the gene is consistently expressed across the different cell or tissue types.

2. A method of claim 1, wherein the R^2 value from the one-factor or two-factor ANOVA analysis is a measure of percent variability of expression for the at least one gene.

3. A method of claim 2, wherein the R^2 value from the one-factor or two-factor ANOVA analysis is less than or equal to about 12.

46. A method of identifying at least one gene that is consistently expressed across different cell or tissue types in an organism or cell line, comprising: (a) querying a gene expression database for the expression level of at least one gene in different cell or tissue types from the organism or cell lines; (b) calculating the percent variability of expression using a one-factor or two-factor ANOVA analysis for said at least one gene across the different cell or tissue types or cell lines; and (c) identifying at least one gene whose percent variability of expression indicates that the gene is consistently expressed across the different cell or tissue types or cell lines.

47. A method of claim 46, wherein the R^2 value from the one-factor or two-factor ANOVA analysis is a measure of percent variability of expression for the at least one gene.

48. A method of claim 47, wherein the R^2 value from the one-factor or two-factor ANOVA analysis is less than or equal to about 12.

Roman et al. in view of Wohlgemuth et al teach the limitations of the base claim on selecting genes that are consistently expressed throughout organs of an organism and there statistical analysis.

Roman et al and Wohlgemuth et al fail to go into detail about use of ANOVA for biostatistics purposes.

However, Michelson et al illustrates in Figure 20 a dot plot of T cell counts, illustrating analysis of variance from Table 15 with R^2 values less than or equal to about

12. the equations on page 85 of Michelson et al. illustrate how to calculate variances and R^2. Variances are shown to be significant statistically through comparison by an F-test statistic on Table 17 of page 81. The F-test statistic acts as a threshold value.

It would have been obvious at the time of the instant invention for someone of ordinary skill in the art to practice Roman et al. in view of Wohlgemuth et al. as applied to claims 1, 4-10, 46, and 49-53 in view of Michelson et al to result in the instantly claimed invention because Michelson et al extends the analysis of Roman et al in view of Wohlgemuth et al. to a more detailed analysis of variance for the analogous problem of adjuvant application on T cells.

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the central PTO Fax Center. The faxing of such pages must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Negin, Ph.D., whose telephone number is (571) 272-1083. The examiner can normally be reached on Monday-Friday from 7am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Andrew Wang, Supervisory Patent Examiner, can be reached at (571) 272-0811.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instrument Examiner, Tina Plunkett, whose telephone number is (571) 272-0549.

Information regarding the status of the application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.. Status information for unpublished applications is available through Private PAIR only. For more information on the PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

-RSN
4 August 2006

4 August 2006

JOHN S. BRUSCA, PH.D
PRIMARY EXAMINER